

We claim:

1. A protein of molecular weight ~~between~~ about 7Kd and about 60Kd, or between about 70Kd and about 200Kd, wherein the protein comprises a thrombospondin-binding motif of HRGP.
2. A pharmaceutical composition comprising a protein which comprises a thrombospondin-binding motif of HRGP, in a pharmaceutically acceptable carrier.
3. The pharmaceutical composition according to claim 2, wherein the composition is produced under GMP conditions or is of clinical grade, or both.
4. A method of modulating the activity of thrombospondin in a tissue comprising: modulating the expression of a protein comprising a thrombospondin-binding motif of HRGP, or modulating the thrombospondin-binding activity of a protein comprising a thrombospondin-binding motif of HRGP.
5. The method according to claim 4, wherein the tissue is a human tissue.
6. The method according to claim 4, wherein the modulation of the activity of thrombospondin in the tissue is a stimulation of the activity of the thrombospondin comprising: inhibiting the expression of the protein comprising a thrombospondin-binding motif of HRGP, or inhibiting the thrombospondin-binding activity of the protein comprising a thrombospondin-binding motif of HRGP.
7. The method according to claim 6, wherein the tissue is a tumor undergoing angiogenesis.
8. The method according to claim 6, wherein the tissue has the characteristics of a cancer selected from the group consisting of: an anal cancer, a bladder cancer, a small cell lung cancer, a non-small cell lung cancer, a bone cancer, a brain cancer, a breast cancer, a cervical cancer, a chondrosarcoma, a clear cell adenocarcinoma

005021 02E0E250

(DES), a colorectal cancer, an endometrial cancer, an esophageal cancer, a cancer of the eye, a cancer of the eyelid, a kaposi's sarcoma, a kidney cancer, a cancer of the larynx, a leiomyosarcoma, a leukemia, a liver cancer, a lung cancer, a lymphoma, a melanoma, a mesothelioma, an oral cancer, an ovarian cancer, a pancreatic cancer, a prostate cancer, a skin cancer, a squamous cell cancer, a stomach cancer, a testicular cancer, a thyroid cancer, a hepatoma, a neuroendocrine cancer, a liposarcoma, a head and neck cancer and a cholangiocarcinoma.

9. The method according to claim 6, wherein the inhibition of the expression of the protein comprising a thrombospondin-binding motif of HRGP is by an HRGP-antisense molecule.
10. The method according to claim 6, wherein the inhibition of the expression of the protein comprising a thrombospondin-binding motif of HRGP is by a ribozyme molecule.
11. The method according to claim 6, wherein the inhibition of HRGP activity is by an antibody with specificity for HRGP, or by an antibody fragment with binding specificity for HRGP.
12. The method according to claim 4 in which the activity of TGF-beta is modulated.
13. The method according to claim 4, wherein the modulation of the activity of thrombospondin in the tissue is an inhibition of the activity of the thrombospondin, comprising: stimulating the expression of HRGP or stimulating the thrombospondin-binding activity of HRGP.
14. The method according to claim 4, wherein the modulation of the activity of thrombospondin in the tissue is a inhibition of the activity of the thrombospondin comprising: inhibiting the activity of thrombospondin in a tissue, comprising increasing the expression of HRGP or increasing the thrombospondin-binding activity of HRGP.

15. The method according to claim 14, wherein the tissue comprises a blood vessel.

16. The method according to claim 15, wherein the blood vessel is a coronary blood vessel.

17. The method according to claim 16, wherein the coronary blood vessel is blocked.

18. The method of claim 16, wherein coronary blood vessel has been treated and restenosis of the blood vessel is prevented.

19. The method according to claim 14 wherein angiogenesis is stimulated.

20. The method according to claim 19 wherein the tissue is a wound tissue.

21. The method of claim 20 wherein the wound tissue is a non-healing diabetic wound tissue.

22. A method of identifying a compound that modulates the thrombospondin-binding activity in sample, said method comprising:

- a) providing a sample that contains a protein with thrombospondin-binding activity,
- b) contacting the sample with a test compound,
- c) assessing the thrombospondin-binding activity of the sample, and
- d) comparing the thrombospondin-binding activity produced by the sample in
 - a) with the thrombospondin-binding activity produced by an identical sample which has not been contacted with the test compound.

23. The method according to claim 22, wherein the sample is a cell sample.

24. The method according to claim 22, wherein the sample is a cell-free sample.

b) The method according claim 22, wherein the sample comprises a protein or peptide that comprises a thrombospondin-binding motif of HRGP.

25. The method of claim 22 in which the thrombospondin -binding activity is assessed by an assay technique selected from the group consisting of: an ELISA, an RIA, an immunohistochemical assay and an in vivo immunoassays.

26. A method of activating tissue plasminogen activator comprising:

- a) contacting the tPA with an immobilized protein comprising a thrombospondin-binding motif of HRGP, or
- b) contacting the tPA with a protein comprising a thrombospondin-binding motif of HRGP and plasminogen; and forming a trimolecular complex of the protein comprising the thrombospondin-binding motif of HRGP with TSP-1 and plasminogen.

27. A method of promoting angiogenesis in the tissues of a mammal comprising administering to the mammal an effective amount of either a) a protein comprising the thrombospondin-binding motif of HRGP, or b) a compound that specifically increases the expression of a protein comprising the thrombospondin-binding motif of HRGP.

28. The method according to claim 27, wherein the protein comprising the thrombospondin-binding motif of HRGP is HRGP.

29. A method of inhibiting tumor proliferation in a mammal comprising administering to the mammal an effective amount of either a) an inhibitor of the binding of the thrombospondin-binding motif of HRGP to TSP-1, or b) a compound that inhibits expression of a protein comprising the thrombospondin-binding motif of HRGP.

30. The method according to claim 29, wherein the inhibitor of the binding of the thrombospondin-binding motif of HRGP to TSP-1 is an antibody that specifically binds HRGP, or a fragment of an antibody that specifically binds HRGP.

31. The method according to claim 29, wherein the compound that inhibits expression of a protein comprising the thrombospondin-binding motif of HRGP is a ribozyme specific for HRGP mRNA.

